

Claims:

1. A method for obtaining a hepatocyte-like cell, comprising:
 - a) providing a stem cell;
 - 5 b) culturing the stem cell in a first medium comprising effective amounts of an acidic fibroblast growth factor (aFGF) and an epidermal growth factor (EGF) for about 2 to 4 days to obtain a first cell population;
 - c) culturing a cell of the first cell population in a second medium comprising an effective amount of hepatocyte growth factor (HGF) for about 2 to 4
10 days to obtain a second cell population; and
 - d) culturing a cell of the second cell population in a third medium comprising effective amounts of oncostatin-M for about 2 to 4 days to obtain a third cell population, the third cell population comprising a plurality of hepatocyte-like cells.
- 15 2. The method of claim 1, wherein the aFGF is present at a concentration of about 1-20 ng/ml and the EGF is present at a concentration of about 1-20 ng/ml in the first medium.
3. The method of claim 1, wherein the HGF is present at a concentration of
20 about 5-50 ng/ml in the second medium.
4. The method of claim 1, wherein the oncostatin-M is present at a concentration of about 1-30 ng/ml in the third medium.
- 25 5. The method of claim 1, further comprising:
 - e) culturing a plurality of cells of the third cell population in a medium suitable for selectively culturing gluconeogenic cells, thereby obtaining a cellular composition comprising an enriched population of hepatocyte-like cells.

6. The method of claim 5, further comprising:

f) culturing a plurality of cells of the enriched population of hepatocyte-like cells in a fifth medium suitable for stimulating hepatocyte-associated metabolic functions, thereby obtaining a cellular composition comprising a population of hepatocyte-like cells having enhanced hepatocyte-associated metabolic activity.

7. The method of claim 6, further comprising:

g) culturing a hepatocyte-like cell in a sixth medium comprising nicotinamide, oncostatin M, dexamethasone, insulin, transferrin and selenium.

10

8. The method of claim 1, further comprising:

e) culturing a plurality of cells of the third cell population in a medium suitable for inducing hepatocyte-like metabolic functions, thereby obtaining a cellular composition comprising a population of hepatocyte-like cells having enhanced hepatocyte-like metabolic activity.

15

9. A method for obtaining a hepatocyte-like cell, comprising:

a) providing an ES cell;
b) stimulating the differentiation of the ES cell into embryoid bodies for about 5 days;

20

c) culturing the embryoid bodies in a first medium comprising effective amounts of an aFGF and an EGF for about 1 to 2 days to obtain embryoid bodies;

25

d) dissociating the embryoid bodies into a single cell suspension and culturing the single cell suspension for about 1 to 2 days in the first medium to obtain a first cell population;

e) culturing a cell of the first cell population in a second medium comprising an effective amount of EGF, HGF and aFGF for about 2 to 4 days to obtain a second cell population; and

f) culturing a cell of the second cell population in a third medium comprising effective amounts of oncostatin-M, EGF, and HGF for about 2 to 4 days to obtain a third cell population, the third cell population comprising a plurality of hepatocyte-like cells.

5

10. A cellular composition comprising viable cells, wherein at least 90% of the viable cells are hepatocyte-like cells.

11. The cellular composition of claim 10, wherein the hepatocyte-like cells:
10 a) use pyruvate as a carbon source;
b) express two or more cytochrome P450 enzymes; and
c) are viable in 5mM butyric acid.

12. A cellular composition obtained by the method of claim 1.

15

13. A cellular composition obtained by the method of claim 9.

14. A method for treating a subject in need of liver cells, comprising administering to the subject a therapeutically effective amount of the hepatocyte-like
20 cells of claim 12.

15. A method for treating a subject in need of liver cells, comprising administering to the subject a therapeutically effective amount of the hepatocyte-like cells of claim 13.

25

16. An isolated nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 18.

17. An isolated polypeptide comprising the amino acid sequence of SEQ ID
NO: 18.